5/7/6
DIALOG(R)File 155:MEDLINE(R)

11664063 99099037 PMID: 9882351
Protection against a lethal avian influenza A virus in a mammalian system.
Riberdy J M; Flynn K J; Stech J; Webster R G; Altman J D; Doherty P C
Department of Immunology, St. Jude Children's Hospital, Memphis, Tennessee 38101, USA.
Journal of virology (UNITED STATES) Feb 1999, 73 (2) p1453-9, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: AI08831; AI; NIAID; AI29579; AI; NIAID; AI38359; AI; NIAID; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The question of how best to protect the human population against a potential influenza pandemic has been raised by the recent outbreak caused by an avian H5N1 virus in Hong Kong. The likely strategy would be to vaccinate with a less virulent, laboratory-adapted H5N1 strain isolated previously from birds. Little attention has been given, however, to dissecting the consequences of sequential exposure to serologically related influenza A viruses using contemporary immunology techniques. Such experiments with the H5N1 viruses are limited by the potential risk to humans. An extremely virulent H3N8 avian influenza A virus has been used to infect both immunoglobulin-expressing (Ig+/+) and Ig-/- mice primed previously with a laboratory-adapted H3N2 virus. The cross-reactive antibody response was very protective, while the recall of CD8(+) T-cell memory in the Ig-/- mice provided some small measure of resistance to a low-dose H3N8 challenge. The H3N8 virus also replicated in the respiratory tracts of the H3N2-primed Ig+/+ mice, generating secondary CD8(+) and CD4(+) T-cell responses that may contribute to recovery. The results indicate that the various components of immune memory operate together to provide optimal protection, and they support the idea that related viruses of nonhuman origin can be used as vaccines.
Record Date Created: 19990218
Record Date Completed: 19990218

3/7/10
DIALOG(R)File 155:MEDLINE(R)

11426696 98309197 PMID: 9645315

Efficacy of inactivated H5N2 influenza vaccines against lethal A/Chicken/Queretaro/19/95 infection.

Garcia A; Johnson H; Srivastava D K; Jayawardene D A; Wehr D R; Webster R G

Department of Virology and Molecular Biology, St. Jude Children's Research Hospital Memphis, TN 38105, USA.

Avian diseases (UNITED STATES) Apr-Jun 1998, 42 (2) p248-56, ISSN 0005-2086 Journal Code: 0370617

Contract/Grant No.: AI-08831; AI; NIAID; CA-21765; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The control and eventual eradication of H5N2 influenza virus from domestic poultry in Mexico is dependent on the use of avian influenza (AI) vaccine strategies. This study was performed to determine the amount of hemagglutinin (HA) antigen required to control the signs of disease from a highly pathogenic H5N2 influenza virus (A/Chicken/ Queretaro/19/95) and the amount of antigen required to prevent shedding of virus from vaccinated birds. Six commercial inactivated water in oil H5N2 vaccines available in Mexico were compared with standardized vaccines to assess their efficacy. The amount of HA required to prevent the signs of disease from A/Chicken/Queretaro/19/95 influenza virus was approximately 0.4 microgram per dose. Each of the six commercially available vaccines prevented disease signs, and half of the vaccines significantly reduced viral shedding from vaccinated birds. There is a need for standardization of AI virus vaccine, and the antigen content should be increased in some of the commercially available AI vaccines in Mexico.

Record Date Created: 19981006

Record Date Completed: 19981006

Trivalent

SF 995.A9 M8

11926575 99370222 PMID: 10438868

Phase 1 evaluation of intranasal virosomal influenza vaccine with and without Escherichia coli heat-labile toxin in adult volunteers.

Gluck U; Gebbers J O; Gluck R

Division of Occupational Medicine, SUVA Swiss National Accident Insurance Institute, CH-6002 Lucerne, Switzerland.

Journal of virology (UNITED STATES) Sep 1999, 73 (9) p7780-6, ISSN 0022-538X Journal Code: 0113724

Document type: Clinical Trial; Clinical Trial, Phase I; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Virosomal vaccines were prepared by extracting hemagglutinin (HA) and neuraminidase from influenza virus and incorporating it in the membranes of liposomes composed of phosphatidylcholine. Two intranasal spray vaccine series were prepared: one series comprised 7.5 micrograms of HA of each of three strains recommended by the World Health Organization and 1 microgram of Escherichia coli heat-labile toxin (HLT), and the other contained the HA without HLT. In addition, a third vaccine preparation contained 15 micrograms of HA and 2 micrograms of HLT. The parenteral virosomal vaccine contained 15 micrograms of HA without additional adjuvant. The immunogenicity of a single spray vaccination (15 micrograms of HA and 2 micrograms of HLT) was compared with that of two vaccinations (7.5 micrograms of HA with or without 1 microgram of HLT) with an interval of 1 week in 60 healthy working adults. Twenty volunteers received one parenteral virosomal vaccine. Two nasal spray vaccinations with HLT-adjuvanted virosomal influenza vaccine induced a humoral immune response which was comparable to that with a single parenteral vaccination. A significantly higher induction of influenza virus-specific immunoglobulin A was noted in the saliva after two nasal applications. The immune response after a single spray vaccination was significantly lower. It could be shown that the use of HLT as a mucosal adjuvant is necessary to obtain a humoral immune response comparable to that with parenteral vaccination. All vaccines were well tolerated.

Record Date Created: 19990907

Record Date Completed: 19990907

9/7/5
DIALOG(R)File 155:MEDLINE(R)

Adonis

10455661 96262419 PMID: 8801083
Comparative analysis of six European influenza vaccines.
Chaloupka I; Schuler A; Marschall M; Meier-Ewert H
Abteilung fur Virologie, Technische Universitat Munchen, Germany.
European journal of clinical microbiology & infectious diseases - official publication of the European Society of Clinical Microbiology (GERMANY) Feb 1996, 15 (2) p121-7, ISSN 0934-9723 Journal Code: 8804297
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Three split-virion vaccines (Vaxigrip, Begrivac, and Influsplit/Fluarix) and three subunit vaccines containing only viral surface glycoproteins (Influvac, Agrippal, and Fluvirin) available for the 1994-95 season were analysed by biological, molecular, and biochemical methods. Although all vaccines are required by health authorities to contain 15 micrograms haemagglutinin per dose of each virus strain, there were significant differences in haemagglutination titres among the examined vaccines of both types. The enzymatic activity of neuraminidase was present in all vaccines except Fluvirin. Total protein content was lower for subunit vaccines. Viral nucleoprotein was detected in all split vaccines but to varying levels according to SDS-PAGE and Western blot analyses. The ovalbumin content was low in general but was about tenfold higher for Influvac than for the other vaccines analysed. This protein may induce hypersensitive reactions among persons with severe egg allergy. All three split-virion vaccines were found to contain the matrix protein; however, it was not detected in the subunit vaccines. Differences in influenza antigen variety in currently available vaccines may affect efficacy, whereas differences in concentrations of nonviral compounds such as ovalbumin and endotoxin may lead to different postvaccination reactogenicity profiles.
Record Date Created: 19961001
Record Date Completed: 19961001

9/7/6
DIALOG(R)File 155:MEDLINE(R)

08425868 95113956 PMID: 7814484

High doses of purified influenza A virus hemagglutinin significantly augment serum and nasal secretion antibody responses in healthy young adults.

Keitel W A; Couch R B; Cate T R; Hess K R; Baxter B; Quarles J M; Atmar R L; Six H R

Acute Viral Respiratory Disease Unit, Baylor College of Medicine, Houston, TX 77030-3498.

Journal of clinical microbiology (UNITED STATES) Oct 1994, 32 (10) p2468-73, ISSN 0095-1137 Journal Code: 7505564

Contract/Grant No.: AI-15103; AI; NIAID; AI-62517; AI; NIAID; RR-00350; RR; NCRR

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The reactogenicity and immunogenicity of purified influenza virus hemagglutinin (HA) vaccines administered intramuscularly were evaluated in two placebo-controlled clinical trials. A total of 139 healthy young adults were randomized to receive increasing doses of monovalent influenza A/Taiwan/1/86 (H1N1) virus HA (range, 0 to 405 micrograms per dose [study 1]). An additional 139 subjects were given increasing doses of a trivalent HA vaccine containing equal amounts of A/H1N1 virus, A/Shanghai/16/89 (H3N2) virus, and influenza B/Yamagata/16/88 virus HA (range, 0 to 135 micrograms of HA per strain, 0 to 405 micrograms per dose) or a standard dose of commercial influenza vaccine (study 2). Increasing doses of HA were associated with increasing frequencies of symptoms at the vaccination site early after vaccination, but all doses were well tolerated. Occurrence of systemic symptoms was unrelated to dose. Increasing the dose of HA resulted in increasingly higher postimmunization levels of serum hemagglutination inhibiting and neutralizing antibody levels versus influenza A/H1N1 virus in study 1 ($P < 0.05$); these enhanced responses persisted for up to 6 months. Nasal secretory immunoglobulin A and G antibody responses were assessed 2 weeks after immunization with monovalent H1N1 virus HA; the frequencies of significant responses also increased in a dose-related fashion. Similar increases in serum antibody levels were noted for both A/H1N1 and A/H3N2 viruses in study 2. These data provide a basis for proceeding with the evaluation of high doses of purified HA in the elderly.

Record Date Created: 19950209

Record Date Completed: 19950209

9/7/7
DIALOG(R)File 155:MEDLINE(R)

QR189.U87
Adonis

07960346 94025897 PMID: 8212831

Efficacy of equine influenza vaccines for protection against A/Equine/Jilin/89 (H3N8)--a new equine influenza virus.

Webster R G; Thomas T L

Department of Virology and Molecular Biology, St Jude Children's Research Hospital Memphis, TN 38101.

Vaccine (ENGLAND) 1993, 11 (10) p987-93, ISSN 0264-410X Journal Code: 8406899

Contract/Grant No.: AI-08831; AI; NIAID; AI-29680; AI; NIAID; CA-21765; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A new H3N8 equine influenza virus [A/Equine/Jilin/1/89 (Eq/Jilin)] appeared in Northeastern China in 1989 and caused high mortality in horses; the available evidence indicates that it has not yet spread outside this region of the world. Serological analysis with postinfection ferret sera in haemagglutination inhibition (HI) tests confirmed that Eq/Jilin is antigenically distinct from H3N8 equine influenza viruses isolated between 1963 and 1991 and also showed that a current equine influenza virus [A/Equine/Alaska/1/91 (H3N8)] had undergone antigenic drift. In the present study we determine if vaccine against a recent H3N8 influenza virus [A/Equine/Kentucky/1277/90 (Eq/Kentucky)] that was standardized for haemagglutinin content will protect mice against lethal challenge with the new H3N8 influenza virus from China. Complete protection is defined as prevention of virus replication in the lungs of mice 3 days after challenge. High doses of Eq/Kentucky vaccine in aqueous suspension (0.5-5.0 micrograms HA per dose) provided minimal protection against Eq/Jilin challenge as judged by virus titres in the lungs of vaccinated animals. Eq/Kentucky vaccine in adjuvant (1.0-5.0 micrograms HA per dose) did provide complete protection against challenge with Eq/Jilin in mice. Eq/Jilin vaccine in aqueous suspension induced complete protection of mice against challenge with Eq/Kentucky at doses from 0.5 to 5 micrograms HA and in adjuvant doses of Eq/Jilin from 0.1-5.0 micrograms HA were efficacious. Homologous protection against Eq/Jilin or Eq/Kentucky was induced by doses of vaccine from 0.5-5.0 micrograms HA per dose in aqueous suspension and from 0.01-5.0 micrograms HA per dose in adjuvant.(ABSTRACT TRUNCATED AT 250 WORDS)

Record Date Created: 19931029

Record Date Completed: 19931029

9/7/9
DIALOG(R)File 155:MEDLINE(R)

04110132 83239795 PMID: 6345659

Studies with inactivated equine influenza vaccine. 1. Serological responses of ponies to graded doses of vaccine.

Wood J M; Mumford J; Folkers C; Scott A M; Schild G C

Journal of hygiene (ENGLAND) Jun 1983, 90 (3) p371-84, ISSN 0022-1724 Journal Code: 0375374

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Serological responses to three bivalent aqueous equine influenza vaccines of different potency and an adjuvanted bivalent vaccine containing inactivated A/equine/Prague/56 (H7N7) and A/equine/Miami/63 (H3N8) viruses, were examined in seronegative ponies. Potencies of the vaccines, measured by single-radial-diffusion tests, ranged from 4 to 56 micrograms of haemagglutinin (HA) antigen activity/virus strain per dose. Serological responses to vaccination were examined by haemagglutination-inhibition (HI) and single-radial-haemolysis (SRH) tests. Four weeks after a primary dose, HI responses to both vaccine viruses were barely detectable; after a second dose the HI responses to A/Miami/63 virus were low or undetectable but HI responses to A/Prague/56 virus were higher (17/20 ponies with titres greater than or equal to 1:16). In contrast SRH tests revealed dose-related antibody responses to both virus strains after one and two vaccine doses; levels after the second dose were 2- to 5-fold higher than after the primary dose. Highest post-vaccination antibody titres were obtained with the adjuvanted vaccine which contained 2- to 4-fold less antigen (13-23 micrograms HA) than the most potent aqueous vaccine. Post-vaccination antibody reacted well in SRH tests with recent antigenic variants of equine influenza virus. A remarkable finding was the high rate of decline in antibody, detected by HI or SRH tests, following one or two doses of vaccine. Even in animals with the highest post-vaccine antibody levels 2-4 weeks after a booster dose, antibody levels had declined to low or indetectable levels 14 weeks later. The low antibody titres detected at 14-32 weeks after vaccination were nevertheless vaccine dose-related.

Record Date Created: 19830826

Record Date Completed: 19830826

9/7/1
DIALOG(R)File 155:MEDLINE(R)

14661372 22346103 PMID: 12458361

Pandemic preparedness: lessons learnt from H2N2 and H9N2 candidate vaccines.

Hehme N; Engelmann H; Kunzel W; Neumeier E; Sanger R
GlaxoSmithKline Biologicals, SSW Dresden, Zirkusstrasse 40, 01069 Dresden, Germany. norbert.w.hehme@gsk.com

Medical microbiology and immunology (Germany) 10 19 2002, 191 (3-4) p203-8, ISSN 0300-8584 Journal Code: 0314524
Document type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Vaccination against influenza is considered to be one of the key interventions in case of a pandemic. Unfortunately, shortages in vaccine supplies will occur because of the substantial increase in vaccine demands worldwide and the limited available supply resources. The recommended use of monovalent--instead of current trivalent--vaccines containing 15 micro g hemagglutinin (HA) per dose can theoretically triple vaccine volumes but is unlikely to meet the demand. Furthermore, previous experiences demonstrated that one dose of 15 micro g HA will not be sufficient to elicit protective antibody levels in unprimed individuals. Modified formulation approaches were investigated, that would be suitable to provide significantly higher volumes of potent vaccine within a given period of time. Low doses of HA combined with aluminum (Al) adjuvants and the use of whole virus instead of split or subunit antigens can lead to substantial increases in process yield. In addition, production of whole virus vaccines will reduce manufacturing complexity. In a dose-finding study in healthy adults and elderly, immune responses after administration of Al-adjuvanted low-dose formulations were compared to a standard split virus vaccine (Fluarix, GlaxoSmithKline Biologicals, Rixensart, Belgium). All vaccines were safe and well tolerated. Antigen concentrations as low as 1.9 micro g HA/strain per dose of adjuvant-containing experimental vaccines induced protective antibody levels in primed populations. Reactogenicity profiles of Al-adjuvanted low-dose vaccines were investigated in a feasibility trial. Neither the use of Al-adjuvant nor of whole virus had a significant effect on general reactions. Studies in unprimed populations with H2N2 and H9N2 candidate vaccines showed different results, with a potential need for a two-dose schedule. Indeed, hemagglutination inhibition titers did not reach protective levels after a single vaccine dose but could be met following administration of a second dose. The same is true for Al-adjuvanted whole virus formulations with an up to eightfold-reduced antigen content. It may be concluded that the use of Al-adjuvanted whole virus vaccines with low HA content can raise protective antibody levels after two vaccine doses, which may, in turn, result in significant increases of vaccine supplies in the case of a pandemic.

Record Date Created: 20021129
Record Date Completed: 20030403

9/7/8
DIALOG(R)File 155:MEDLINE(R)

11029066 97382689 PMID: 9240693
Improvement of inactivated influenza virus vaccines.
Couch R B; Keitel W A; Cate T R
Baylor College of Medicine, Department of Microbiology and Immunology, Houston, Texas 77030, USA.
Journal of infectious diseases (UNITED STATES) Aug 1997, 176 Suppl 1 pS38-44, ISSN 0022-1899 Journal Code: 0413675
Contract/Grant No.: AI-15103; AI; NIAID
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Inactivated influenza virus vaccines (IVVs) are used for prevention of influenza and its complications. Present vaccines are immunogenic, of low reactogenicity, and protective, but protection has varied between 0% and 100%. Increasing the dose of hemagglutinin and neuraminidase antigens with purified proteins significantly increased serum and nasal antibody responses; however, trials with newer adjuvants have not shown increased serum antibody to levels comparable with those in earlier studies using oil emulsion adjuvants. IgA antibody responses in respiratory secretions were enhanced by the respiratory administration of IVVs, but IVVs by the oral route yielded varying results. IVVs appeared less effective for pandemic influenza in 1968 than in 1957. Since IVVs will be the major preventative measure for pandemic influenza in most countries, they need to be improved to provide better protection against pandemic and interpandemic influenza. Increasing the doses of hemagglutinin and neuraminidase, using adjuvants or immunomodulators, and administering IVVs by the mucosal route could improve the performance of these vaccines. (49 Refs.)
Record Date Created: 19970814
Record Date Completed: 19970814